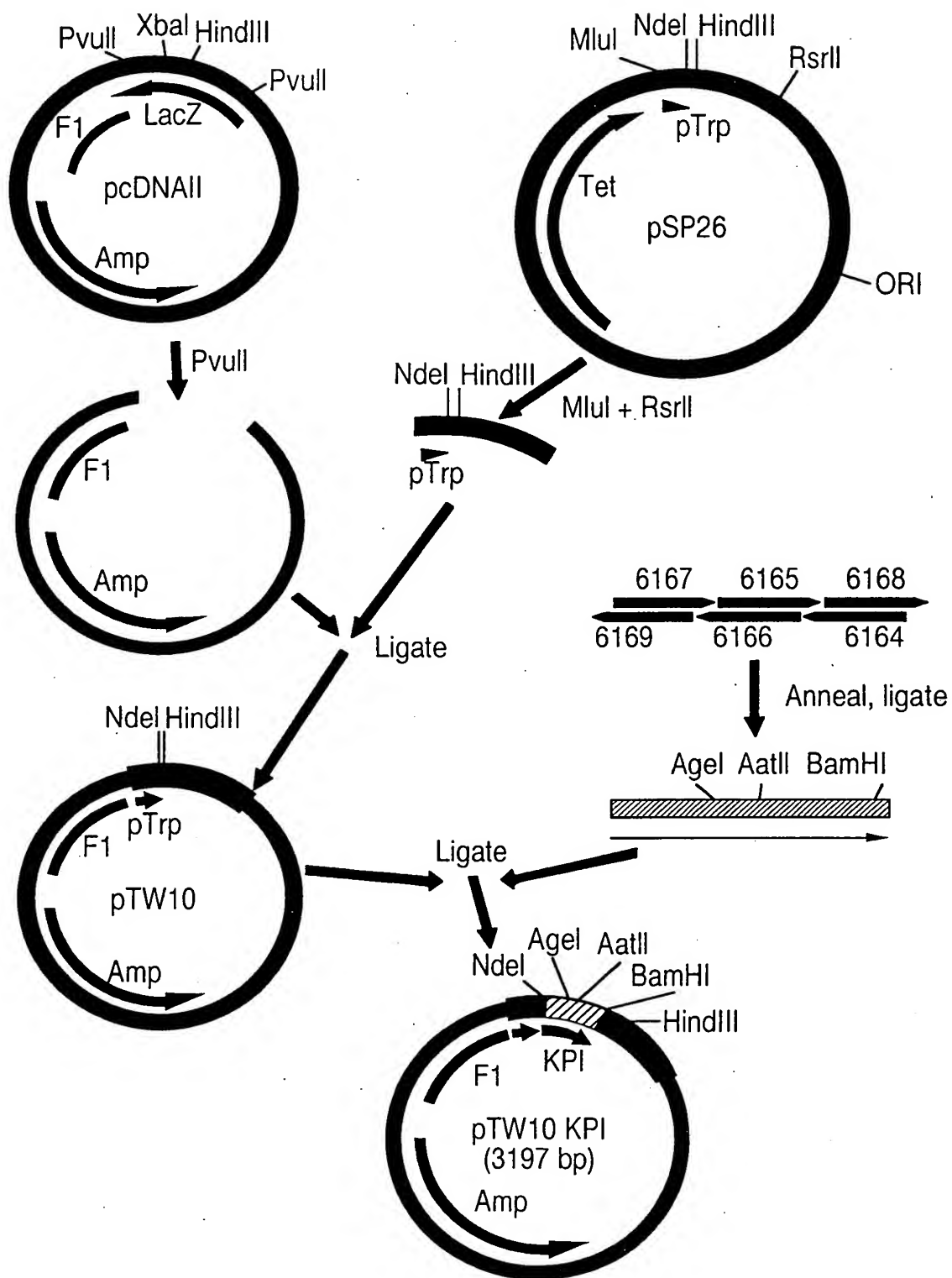


FIG. 1





Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 10/076,604

FIG. 2

NdeI

TATG AAA CAA AGC ACT ATT GCA CTG GCA CTC TTA CCG TTA CTG TTT ACC CCT GTG ACA AAA
AC TTT GTT TCG TGA TAA CGT GAC CGT GAG AAT GGC AAT GAC AAA TGG GGA CAC TGT TTT
▶ Met Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr Pro Val Thr Lys

KPI

AgeI

GCC GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT GCA ATG ATC TCC CGC TGG
CGG CTC CAC ACG AGA CTT GTT CGA CTC TGG CCA GGC ACG GCA CGT TAC TAG AGG GCG ACC
▶ Ala Glu Val Cys Ser Glu Glu Ala Glu Thr Gly Pro Cys Arg Ala Met Ile Ser Arg Trp

AatII

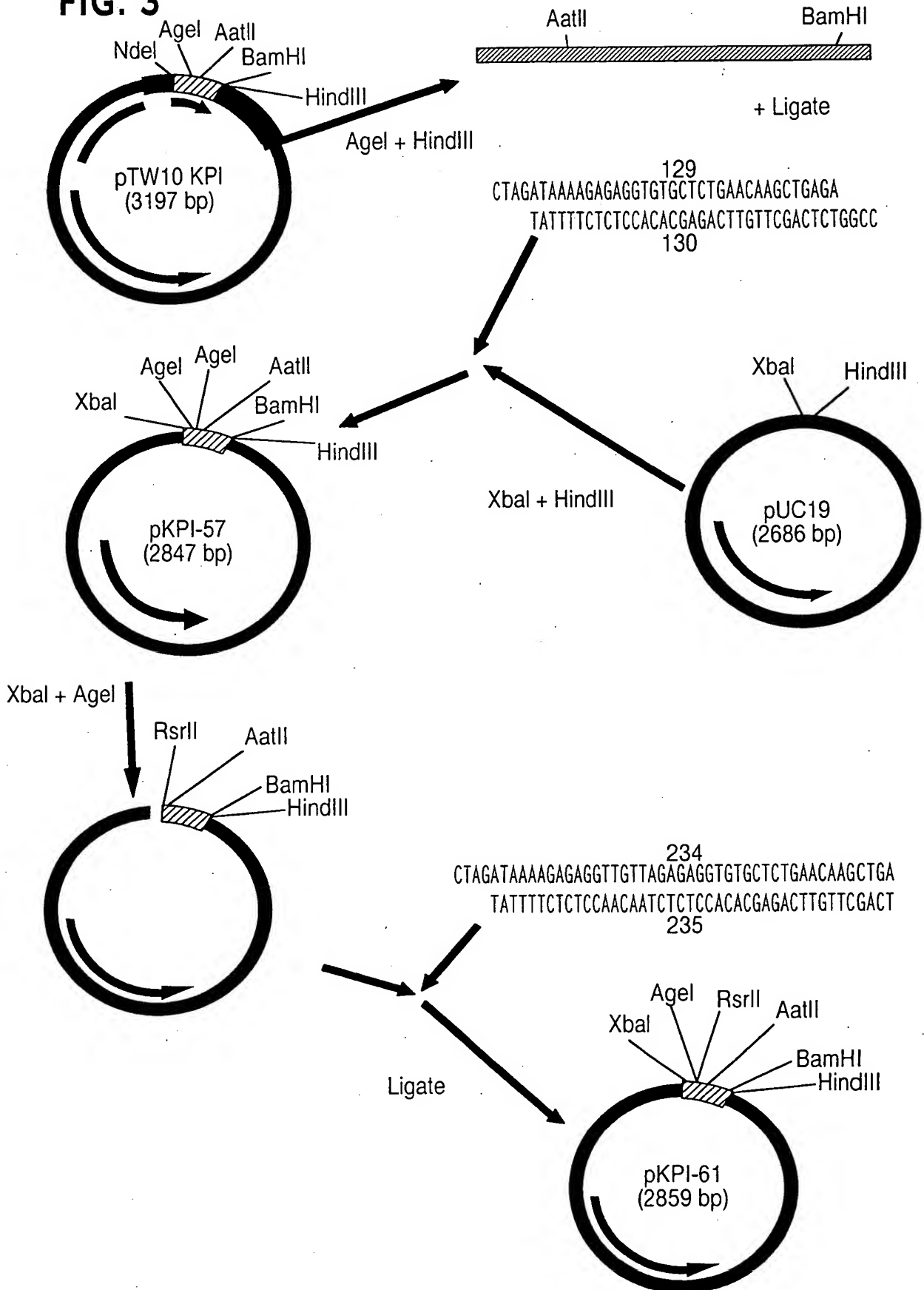
TAC TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC AAC
ATG AAA CTG CAG TGA CTT CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG
▶ Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Tyr Gly Gly Cys Gly Gly Asn

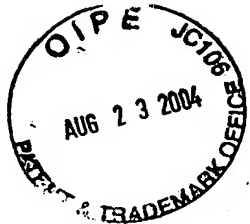
BamHI

HindIII

CGT AAC AAC TTT GAC ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TA
GCA TTG TTG AAA CTG TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA
▶ Arg Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

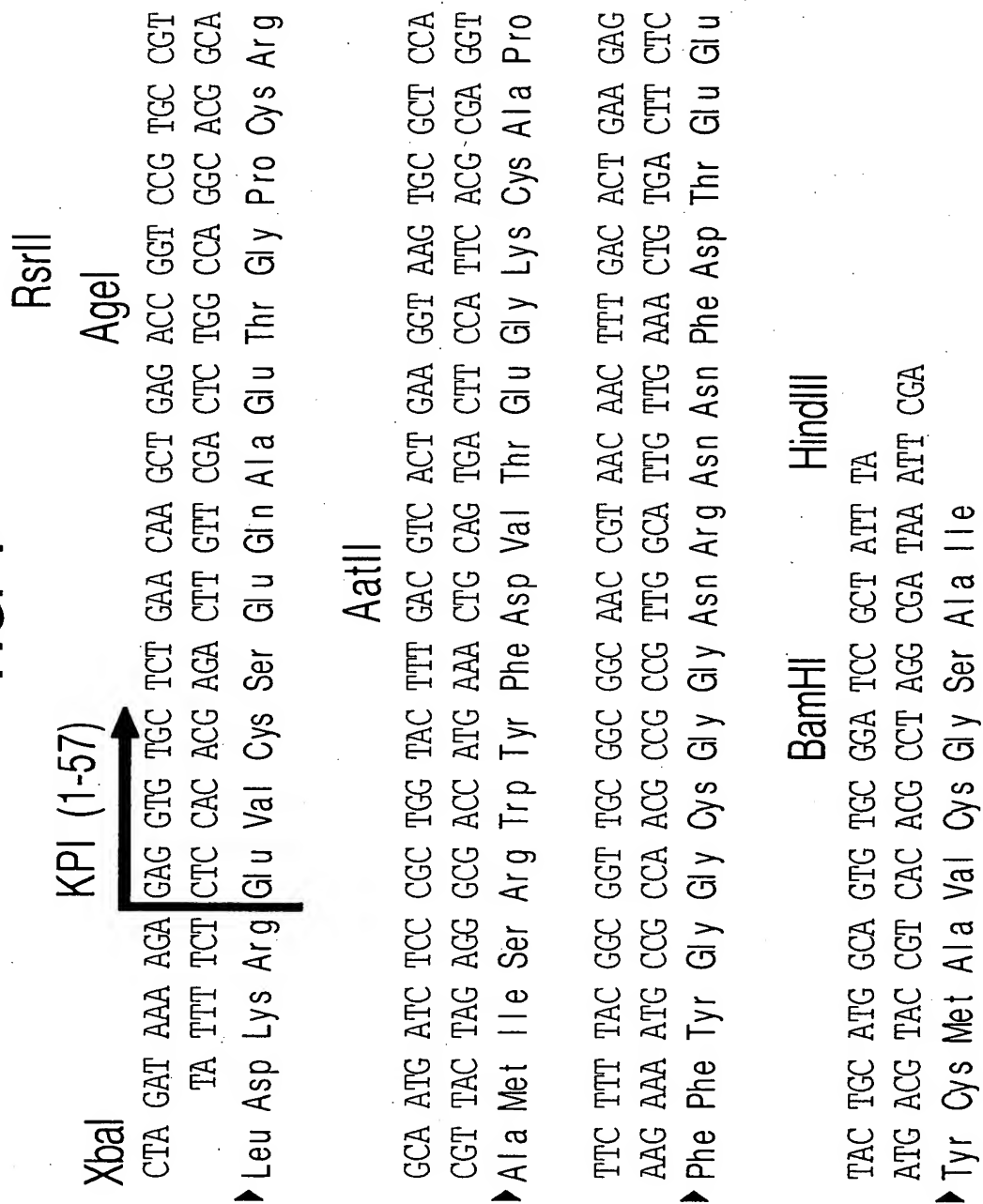
FIG. 3





Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 10/076,604

FIG. 4





Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 10/076,604

FIG. 5

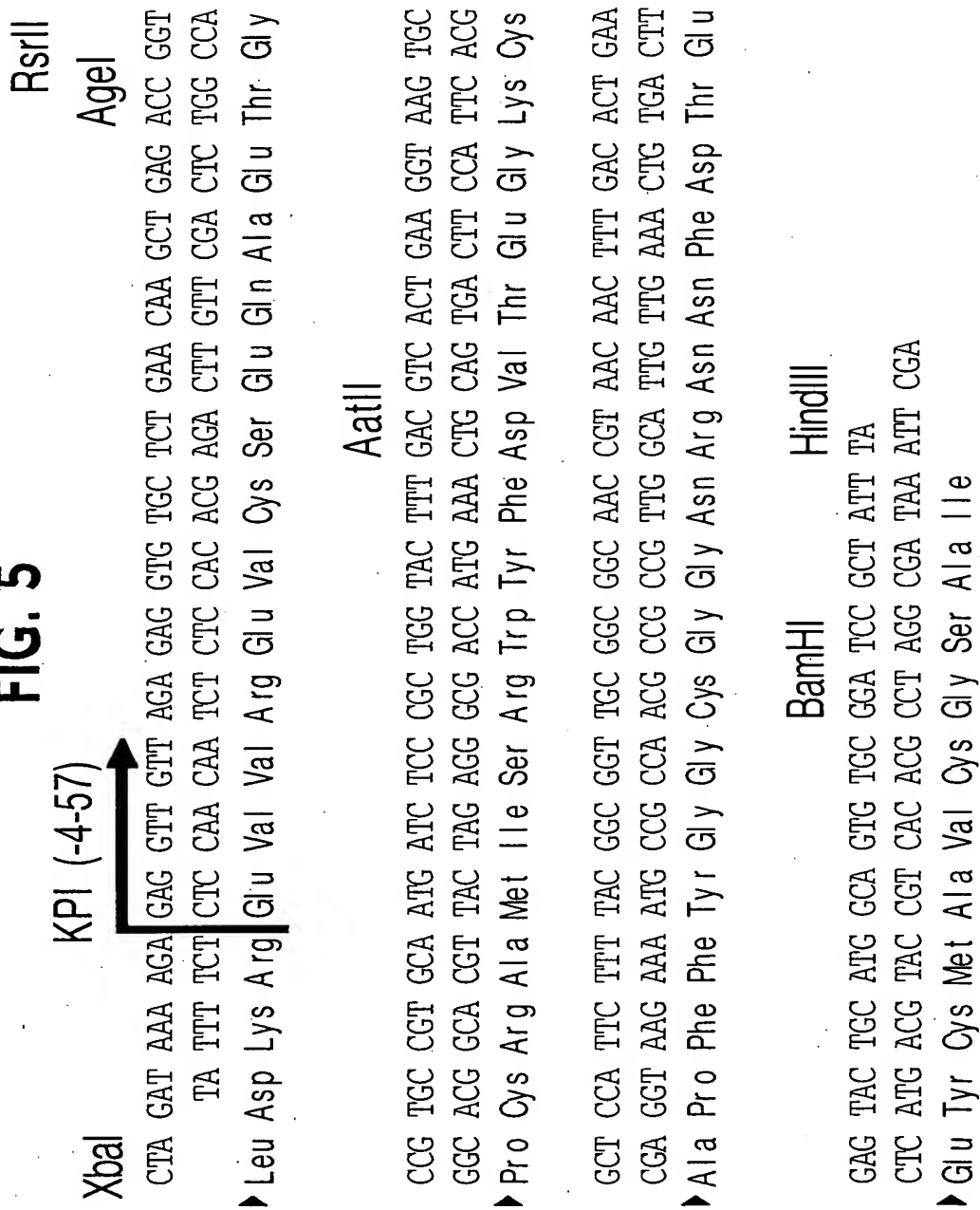
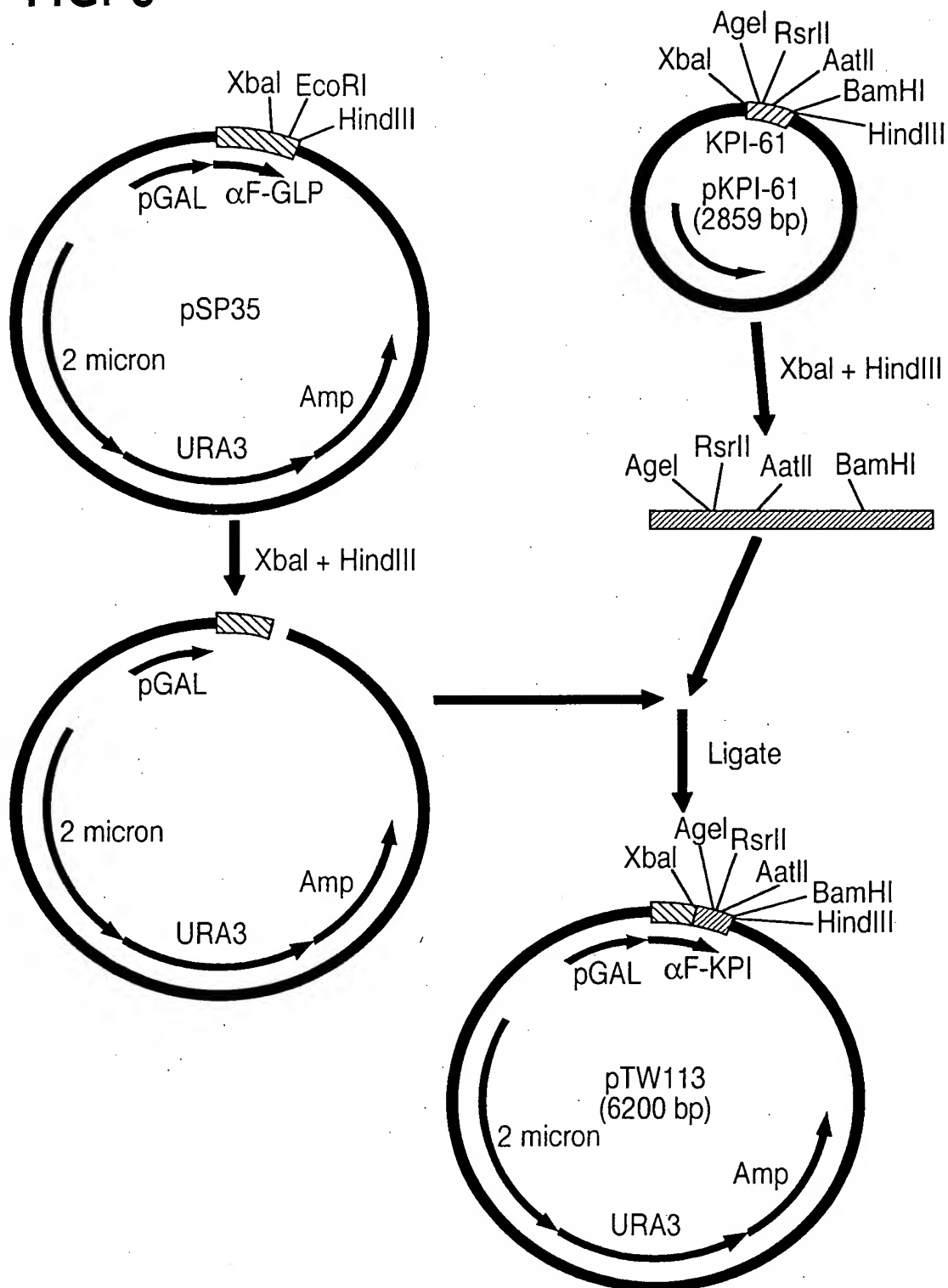


FIG. 6





Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 10/076,604

FIG. 7

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA ATG ATC TCC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT TAC TAG AGG GCG ACC ATG AAA CTG CAG TGA CTT
▶ Ala Glu Thr Gly Pro Cys Arg Ala Met Ile Ser Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 10/076,604

FIG. 8

KPI(-4-57)

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - Ile - Ser - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57

FIG. 9

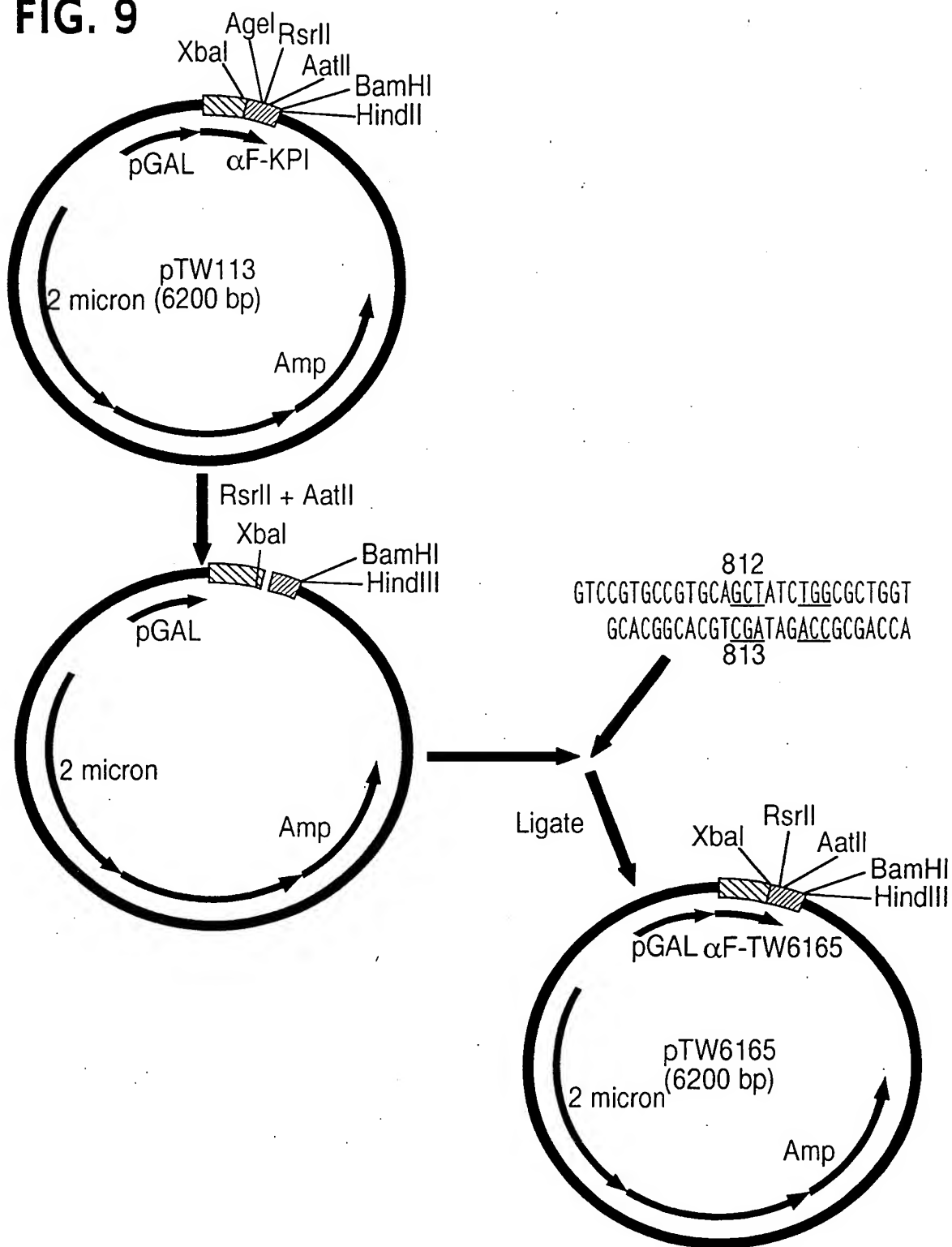




FIG. 10

pTW 6165

α -factor

→
ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A, S17W)

→
GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TGG CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT CGA TAG ACC GCG ACC ATG AAA CTG CAG TGA CTT
▶ Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Trp Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



FIG. 11

812	GTCCGTGCGGTGCAGCTATCTGGCGCTGGTACTTTGACGT GCACGGCAOGT <u>CGATAGACGGG</u> GAOCATGAAAC	pTW6165 KPI(-4-57; M15A, S17F)
813		
814	GTCCGTGCGGTGCAGCTATCTACCGCTGGTACTTTGACGT GCACGGCAOGT <u>CGATAGATGGG</u> GAOCATGAAAC	pTW6166 KPI(-4-57; M15A, S17Y)
815		
867	GTCCGTGCGGTGCATTGATCTTCCGCTGGTACTTTGACGT GCACGGCAOGT <u>AACTAGAAGGG</u> GAOCATGAAAC	pTW6175 KPI(-4-57; M15L, S17F)
868		
1493	GTCCGTGCGGTGCATTGATCTACCGCTGGTACTTTGACGT GCACGGCAOGT <u>AACTAGATGGG</u> GAOCATGAAAC	pBG028 KPI(-4-57; M15L, S17Y)
1494		
925	GTCCGTGCGGTGCAATGCACTTCCGCTGGTACTTTGACGT GCACGGCAOGTTAOGTGAAGGGGAOCATGAAAC	pTW6183 KPI(-4-57; I16H, S17F)
926		
927	GTCCGTGCGGTGCAATGCACTACCGCTGGTACTTTGACGT GCACGGCAOGTTAOGTGATGGGGAOCATGAAAC	pTW6184 KPI(-4-57; I16H, S17Y)
928		
929	GTCCGTGCGGTGCAATGCACTGGCGCTGGTACTTTGACGT GCACGGCAOGTTAOGTGAAGGGGAOCATGAAAC	pTW6185 KPI(-4-57; I16H, S17W)
930		
863	GTCCGTGCGGTGCAGCTCACTCCCGCTGGTACTTTGACGT GCACGGCAOGT <u>CGAGTGAGGGG</u> GAOCATGAAAC	pTW6173 KPI(-4-57; M15A, I16H)
864		
865	GTCCGTGCGGTGCATTGCACTCCCGCTGGTACTTTGACGT GCACGGCAOGT <u>AAAGTGAGGGG</u> GAOCATGAAAC	pTW6174 KPI(-4-57; M15L, I16H)
866		



FIG. 12

pTW 6166

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA

► Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG

► Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG

► Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT

► Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A, S17Y)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT

► Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TAC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT CGA TAG ATG GCG ACC ATG AAA CTG CAG TGA CTT

► Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Tyr Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG

► Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A

► Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



FIG. 13

pTW 6175

α -factor

→
ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI
KPI(-4-57; M15L, S17F)
→
GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII
AgeI
AatII
GCT GAG ACC GGT CCG TGC CGT GCA TTG ATC TTC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT AAC TAG AAG GCG ACC ATG AAA CTG CAG TGA CTT
▶ Ala Glu Thr Gly Pro Cys Arg Ala Leu Ile Phe Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI
HindIII
ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

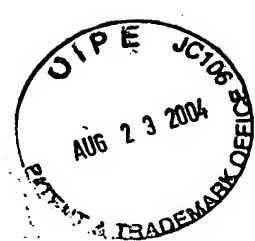


FIG. 14

pBG028

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15L, S17Y)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA TTG ATC TAC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT AAC TAG ATG GCG ACC ATG AAA CTG CAG TGA CTT
▶ Ala Glu Thr Gly Pro Cys Arg Ala Leu Ile Tyr Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



FIG. 15

pTW6183

α -factor

→
ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

KPI(-4-57; I16H, S17F)

XbaI

→
GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

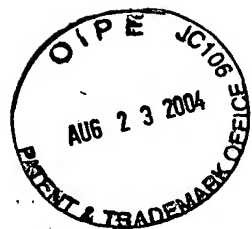
GCT GAG ACC GGT CCG TGC CGT GCA ATG CAC TTC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT TAC GTG AAG GCG ACC ATG AAA CTG CAG TGA CTT
▶ Ala Glu Thr Gly Pro Cys Arg Ala Met His Phe Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



pTW6184

FIG. 16

α -factor

→
ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; I16H, S17Y)

→
GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA ATG CAC TAC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT TAC GTG ATG GCG ACC ATG AAA CTG CAG TGA CTT
▶ Ala Glu Thr Gly Pro Cys Arg Ala Met His Tyr Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



pTW6185

FIG. 17

α -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; I16H, S17W)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA ATG CAC TGG CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT TAC GTG ACC GCG ACC ATG AAA CTG CAG TGA CTT
Ala Glu Thr Gly Pro Cys Arg Ala Met His Trp Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



pTW6173

FIG. 18

α -factor

→
ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A, I16H)

→
GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT CAC TCC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT CGA GTG AGG GCG ACC ATG AAA CTG CAG TGA CTT
▶ Ala Glu Thr Gly Pro Cys Arg Ala Ala His Ser Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



pTW6174

FIG. 19

α -factor

→
ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15L, I16H)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

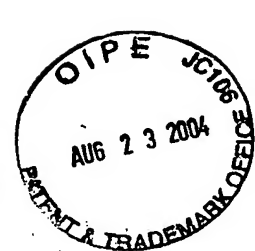
GCT GAG ACC GGT CCG TGC CGT GCA TTG CAC TCC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT AAC GTG AGG GCG ACC ATG AAA CTG CAG TGA CTT
▶ Ala Glu Thr Gly Pro Cys Arg Ala Leu His Ser Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



Title: PROTEASE INHIBITOR
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Inventor(s): R. Tyler WHITE et al.
Appl. No.: 10/076,604

FIG. 20

KPI(-4-57; M15A, S17W) TW6165

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

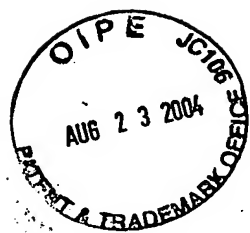
Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - Ile - Trp - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57



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Appl. No.: 10/076,604

FIG. 21

KPI(-4-57; M15A, S17Y) TW6166

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - Ile - Tyr - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57



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Inventor(s): R. Tyler WHITE et al.
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FIG. 22

KPI(-4-57; M15L, S17F) TW6175

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

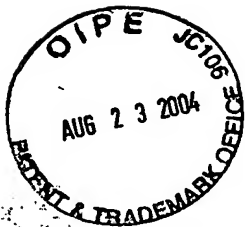
Glu - Thr - Gly - Pro - Cys - Arg - Ala - Leu - Ile - Phe - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57



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Appl. No.: 10/076,604

FIG. 23

KPI(-4-57; M15L, S17Y) BG028

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Leu - Ile - Tyr - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57



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Appl. No.: 10/076,604

FIG. 24

KPI(-4-57; I16H, S17F) TW6183

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - His - Phe - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57



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PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 10/076,604

FIG. 25

KPI(-4-57; I16H, S17Y) TW6184

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - His - Tyr - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57



Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 10/076,604

FIG. 26

KPI(-4-57; I16H, S17W) TW6185

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

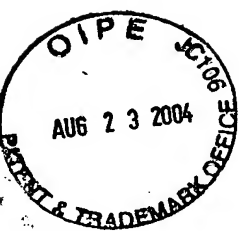
Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - His - Trp - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57



Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 10/076,604

FIG. 27

KPI(-4-57; M15A, S17F) DD185

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - Ile - Phe - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57



Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 10/076,604

FIG. 28

KPI(-4-57; M15A, I16H) TW6173

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - His - SerTrp - Arg
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile
52 53 54 55 56 57



Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 10/076,604

FIG. 29

KPI(-4-57; M15L, I16H) TW6174

Glu	-	Val	-	Val	-	Arg	-	Glu	-	Val	-	Cys	-	Ser	-	Glu	-	Gln	-	Ala
-4		-3		-2		-1		1		2		3		4		5		6		7

Glu	-	Thr	-	Gly	-	Pro	-	Cys	-	Arg	-	Ala	-	<u>Leu</u>	-	<u>His</u>	-	Ser	-	Arg
8		9		10		11		12		13		14		15		16		17		18

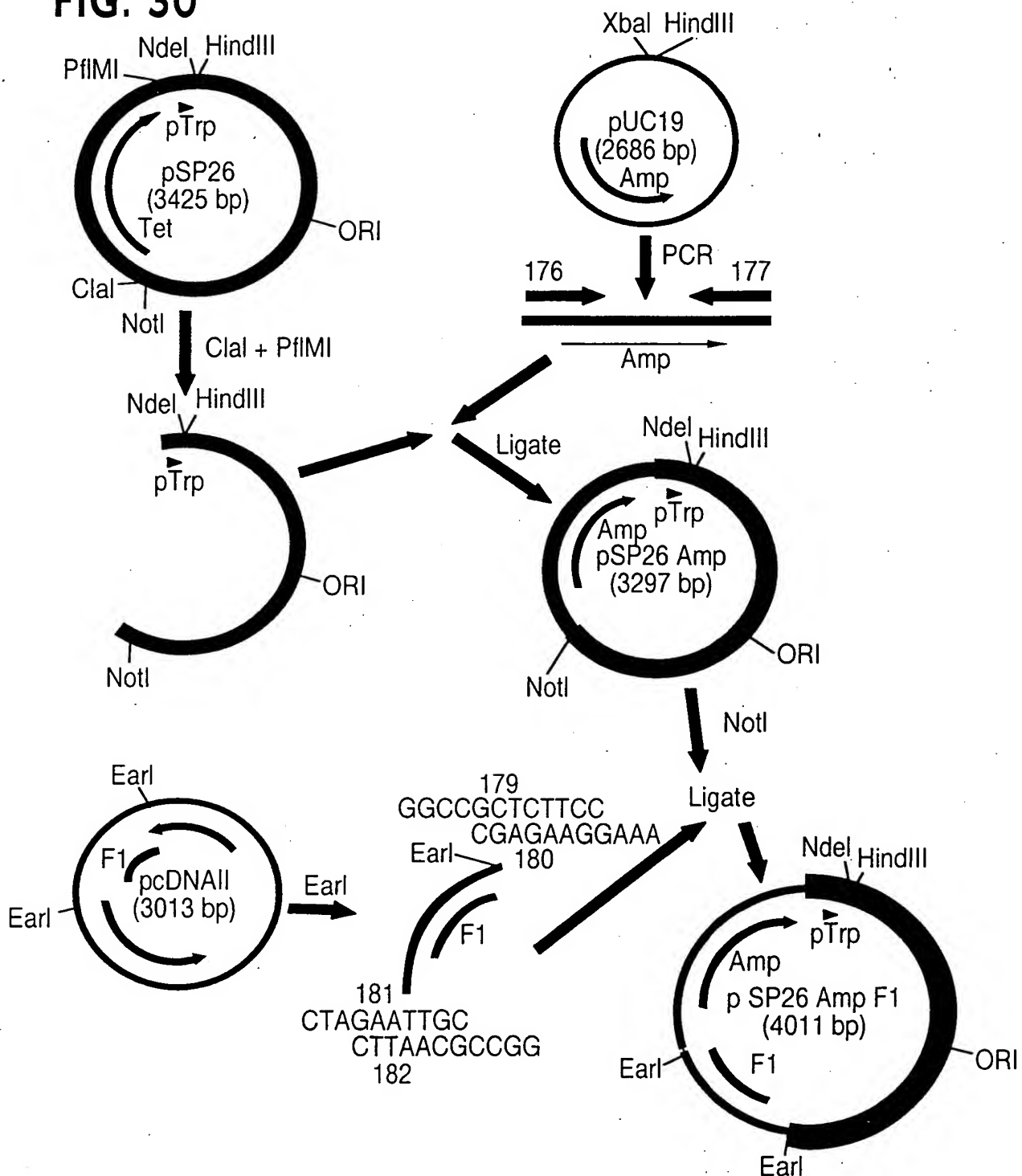
Trp	-	Tyr	-	Phe	-	Asp	-	Val	-	Thr	-	Glu	-	Gly	-	Lys	-	Cys	-	Ala
19		20		21		22		23		24		25		26		27		28		29

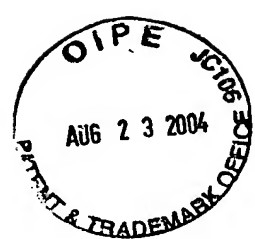
Pro	-	Phe	-	Phe	-	Tyr	-	Gly	-	Gly	-	Cys	-	Gly	-	Gly	-	Asn	-	Arg
30		31		32		33		34		35		36		37		38		39		40

Asn	-	Asn	-	Phe	-	Asp	-	Thr	-	Glu	-	Glu	-	Tyr	-	Cys	-	Met	-	Ala
41		42		43		44		45		46		47		48		49		50		51

Val	-	Cys	-	Gly	-	Ser	-	Ala	-	Ile
52		53		54		55		56		57

FIG. 30





Title: PROTEASE INHIBITOR
PEPTIDES
Inventor(s): R. Tyler WHITE et al.
Appl. No.: 10/076,604

FIG. 31

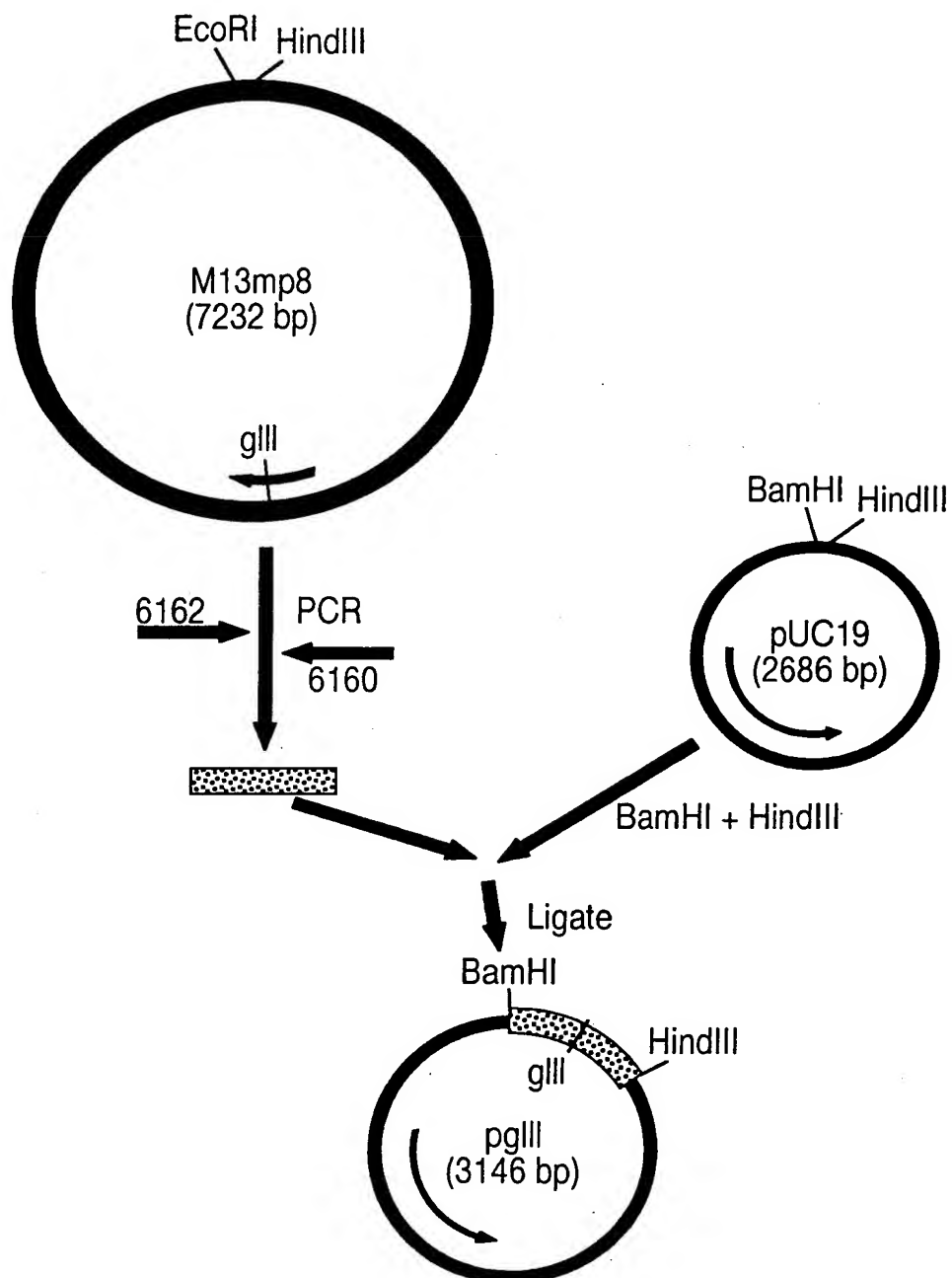


FIG. 32

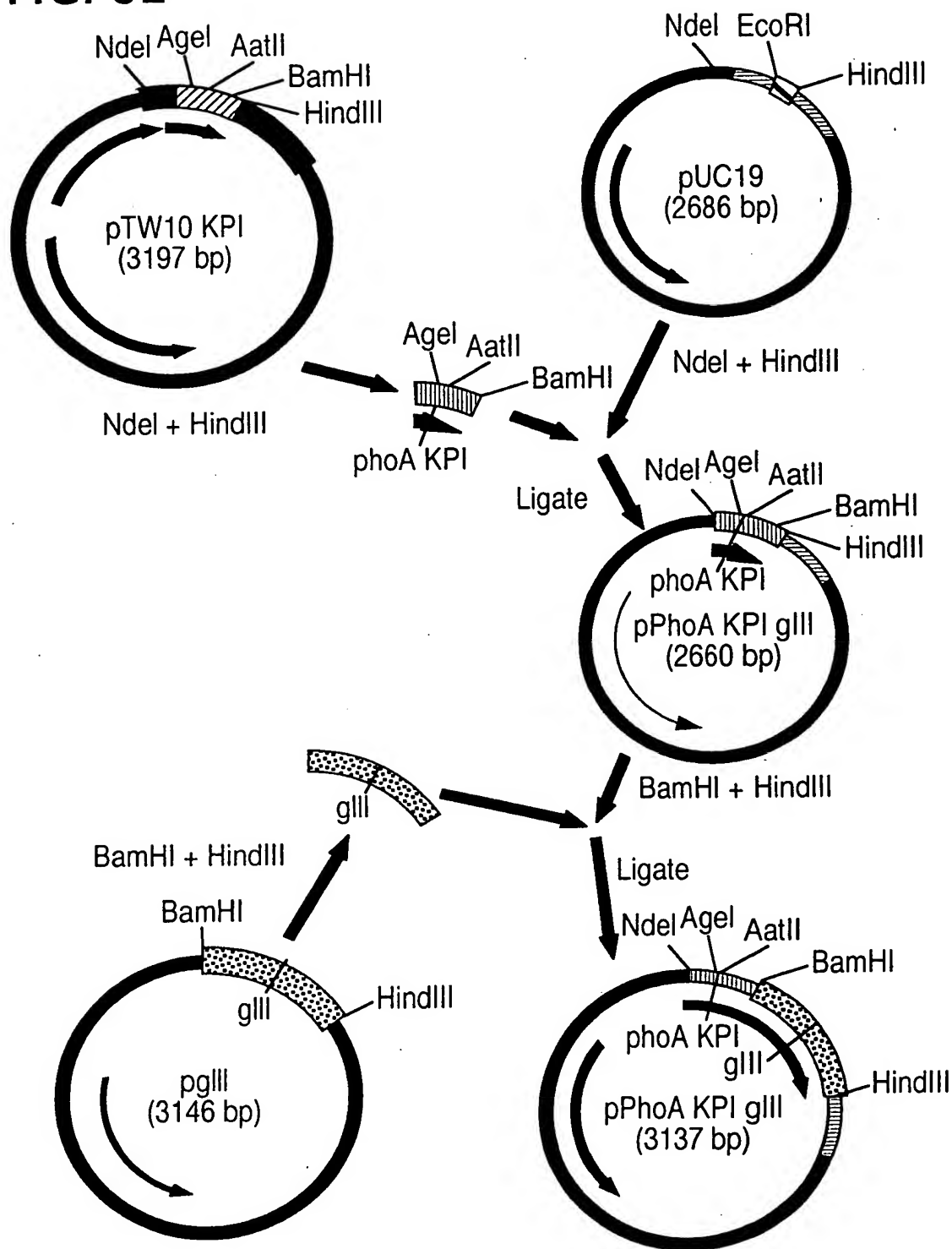


FIG. 33

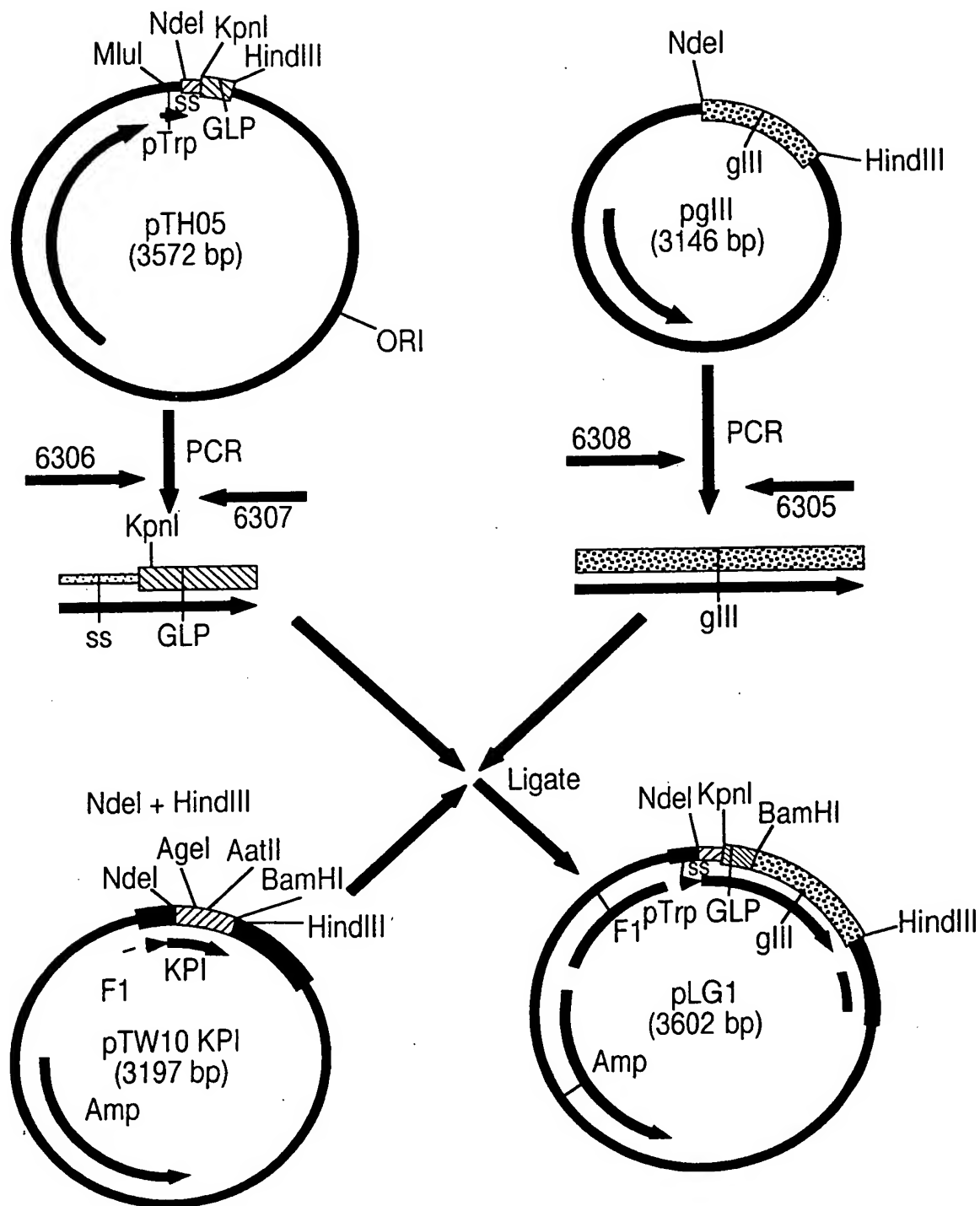


FIG. 34

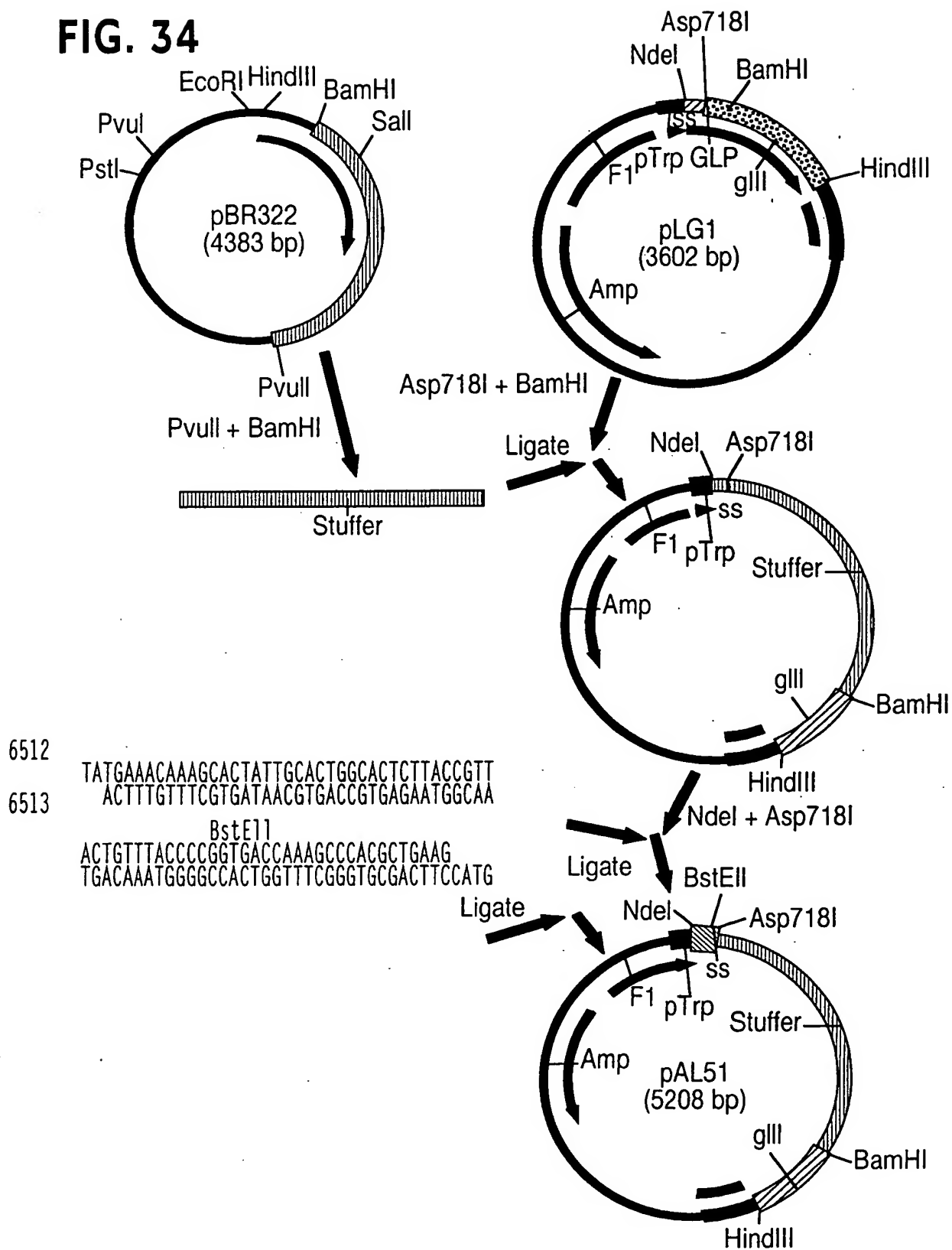




FIG. 35

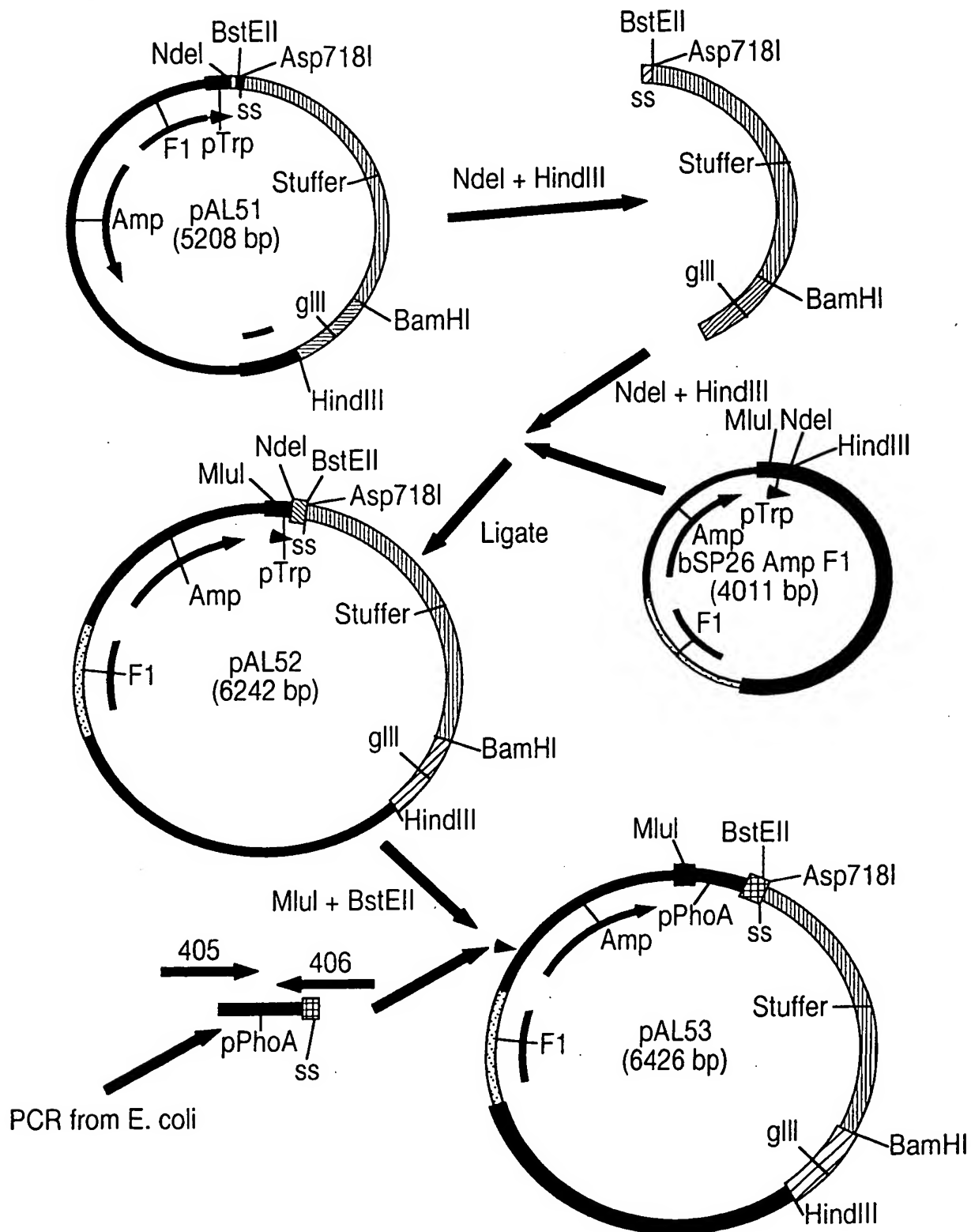


FIG. 36

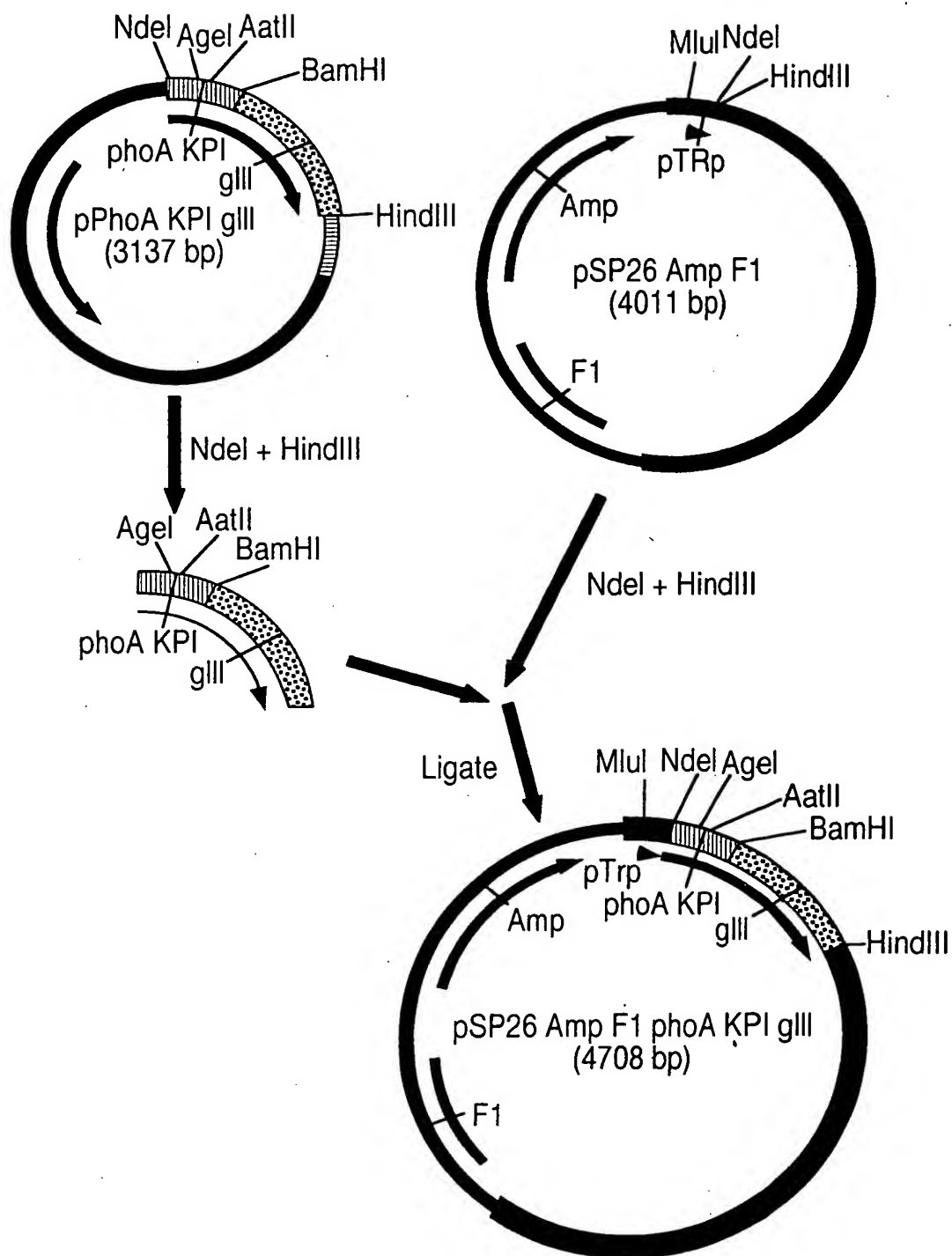


FIG. 37

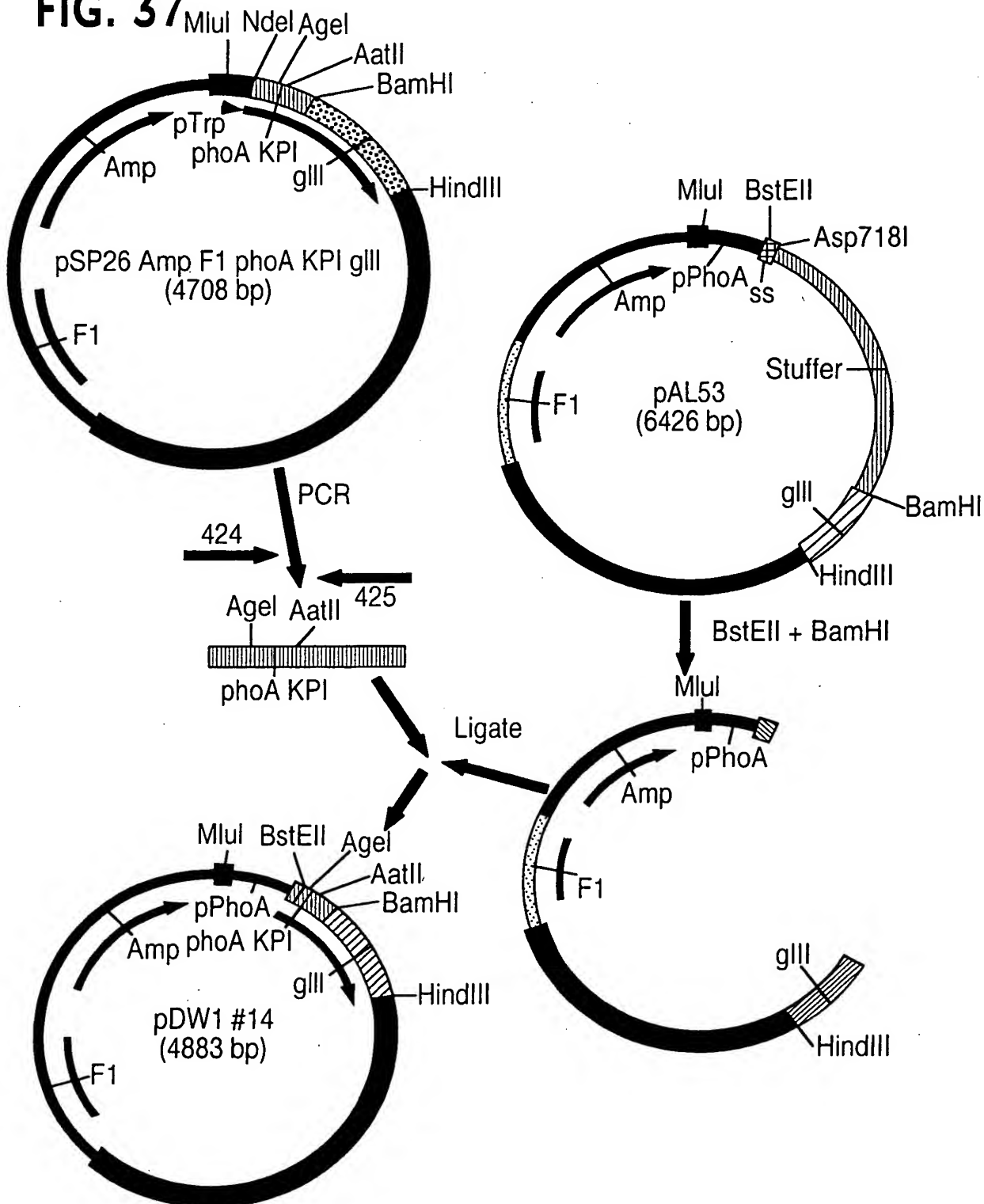




FIG. 38

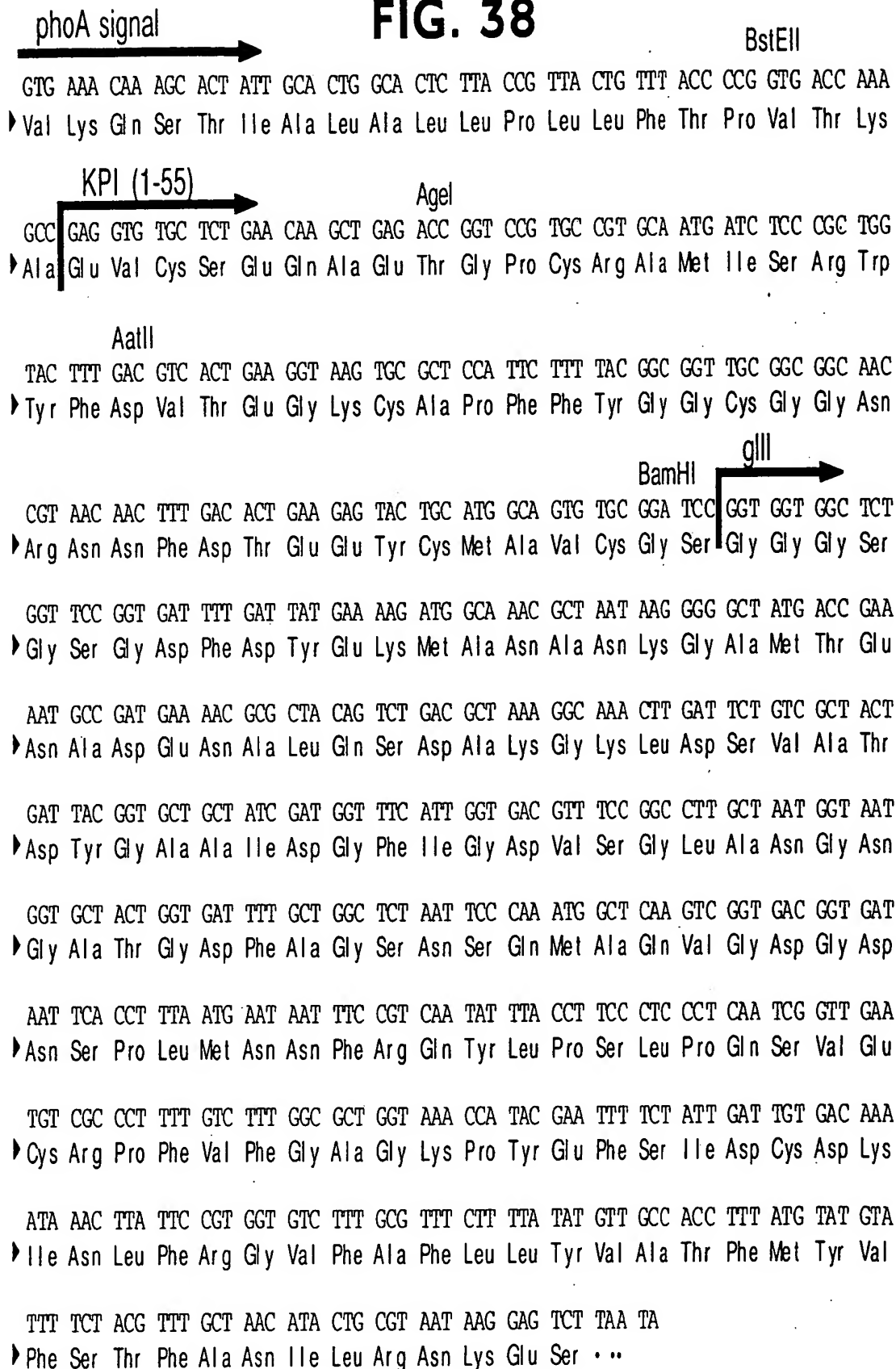


FIG. 39

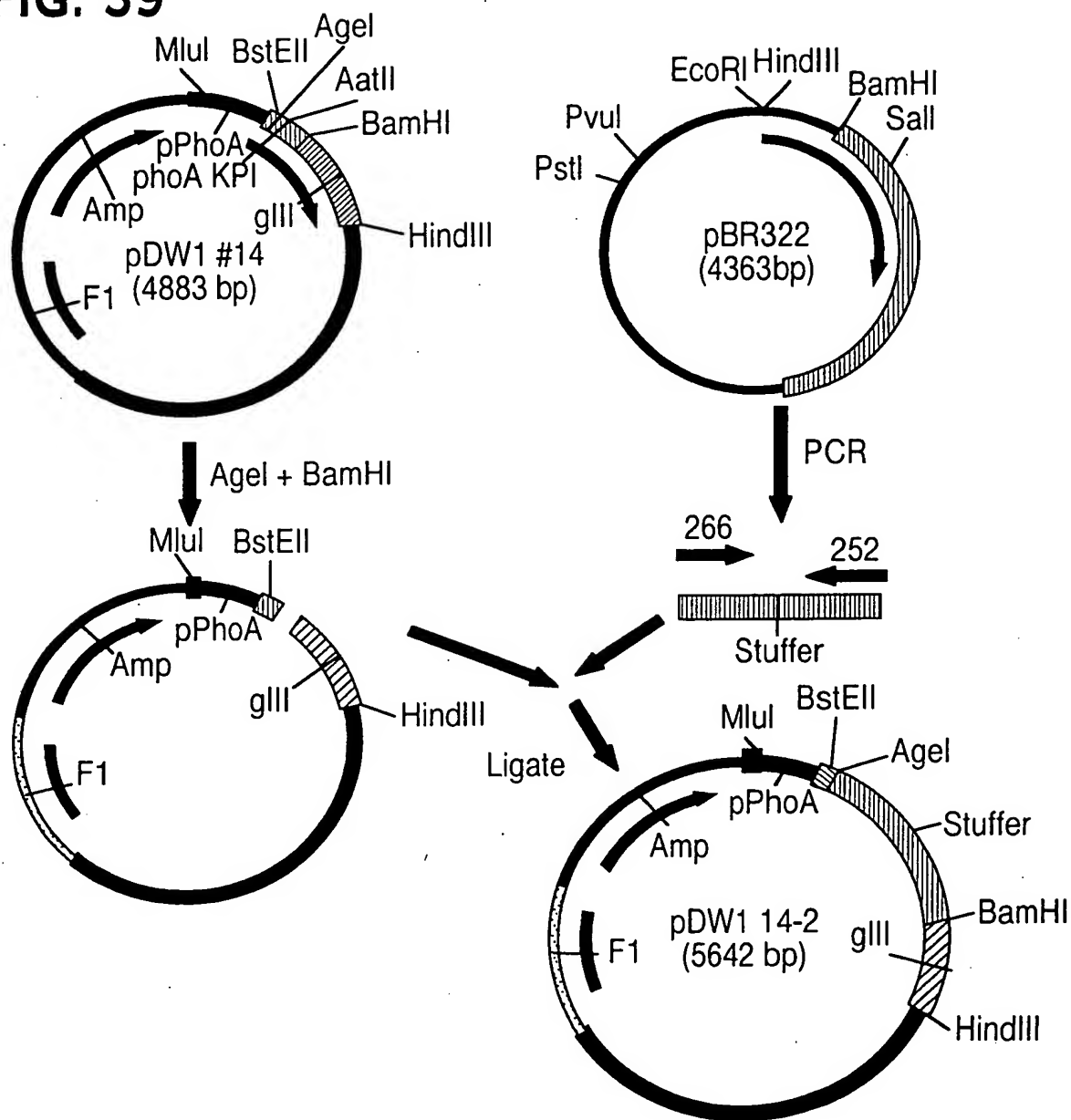
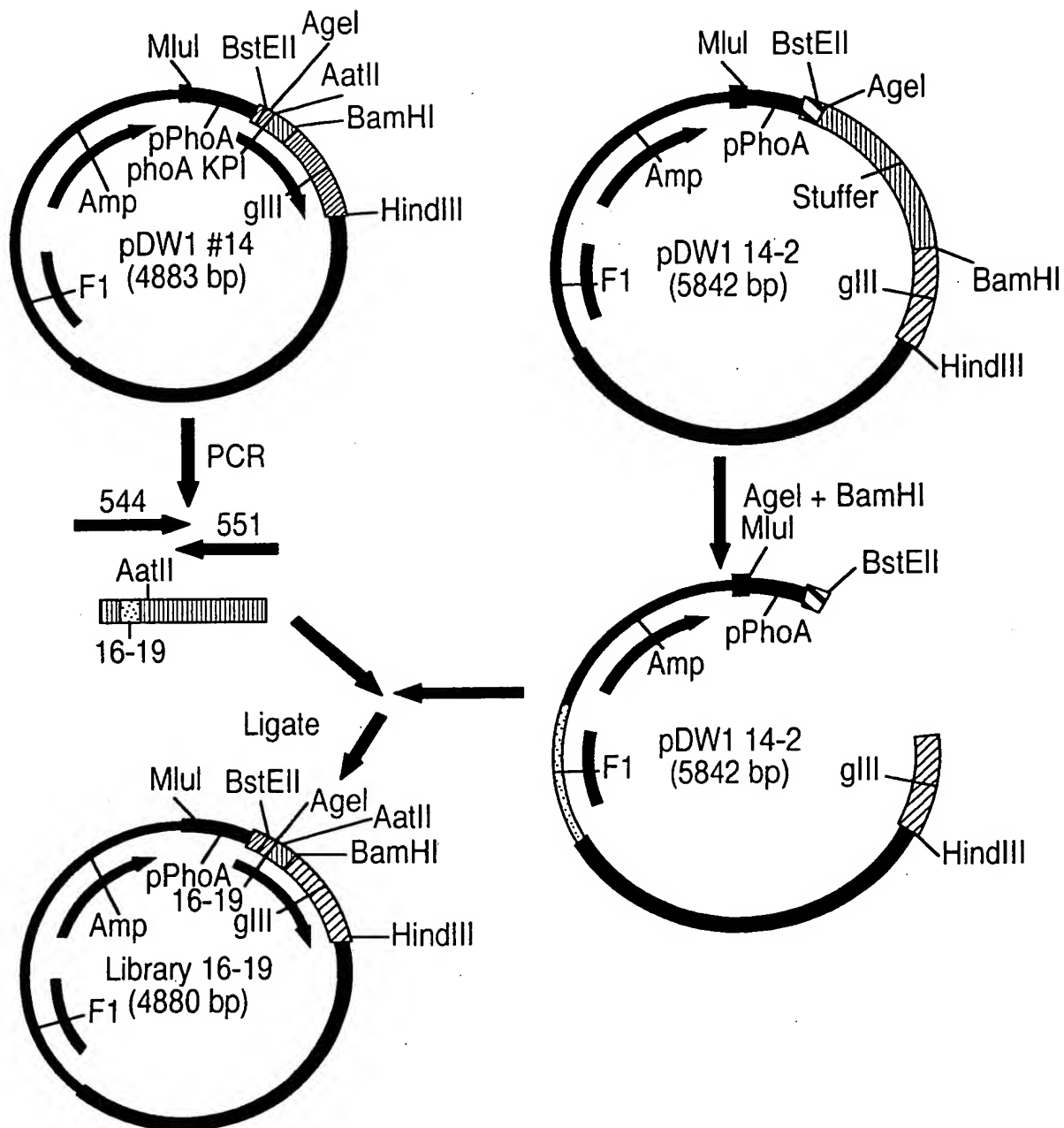


FIG. 40





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Appl. No.: 10/076,604

FIG. 41

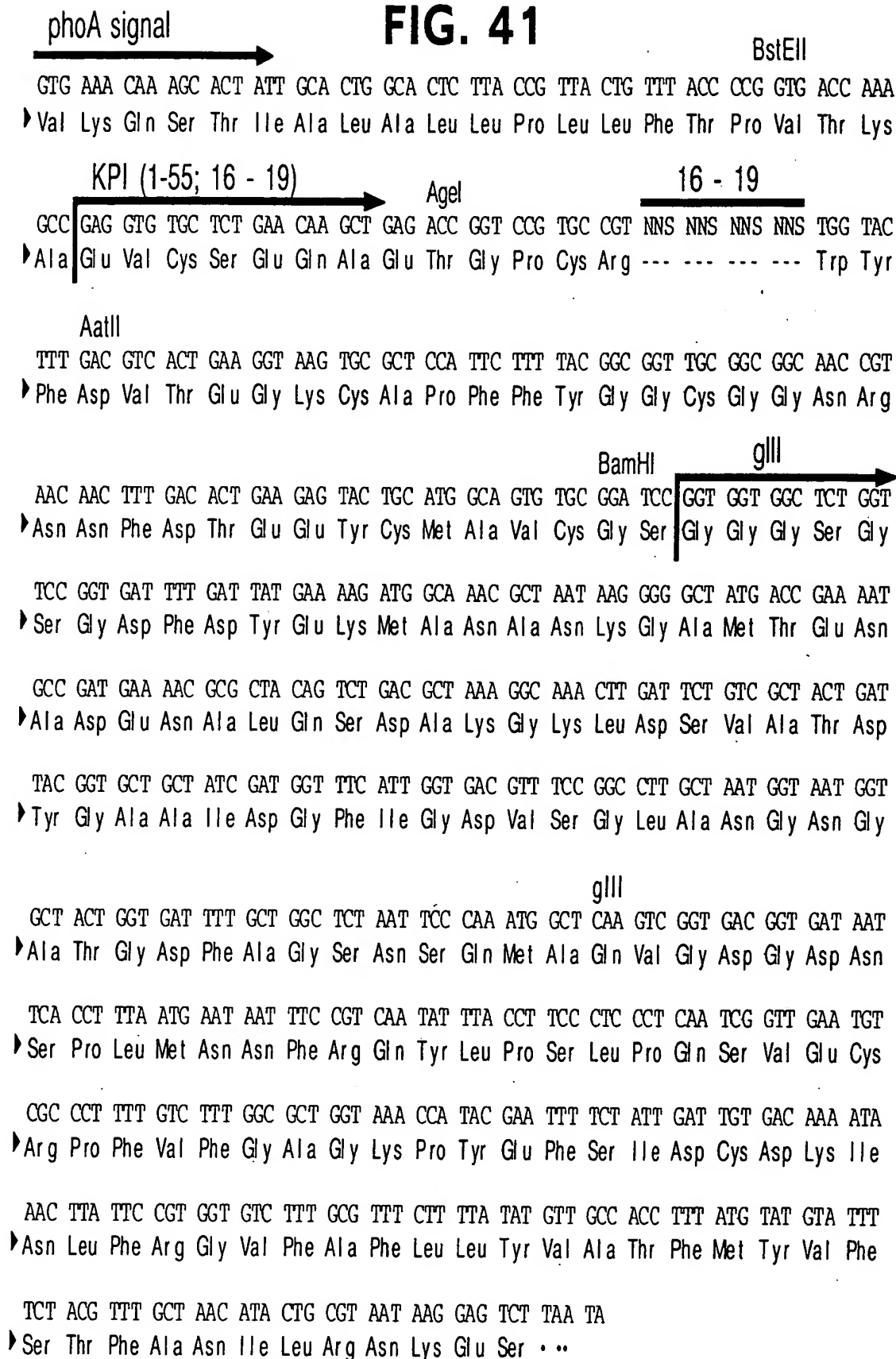




FIG. 42

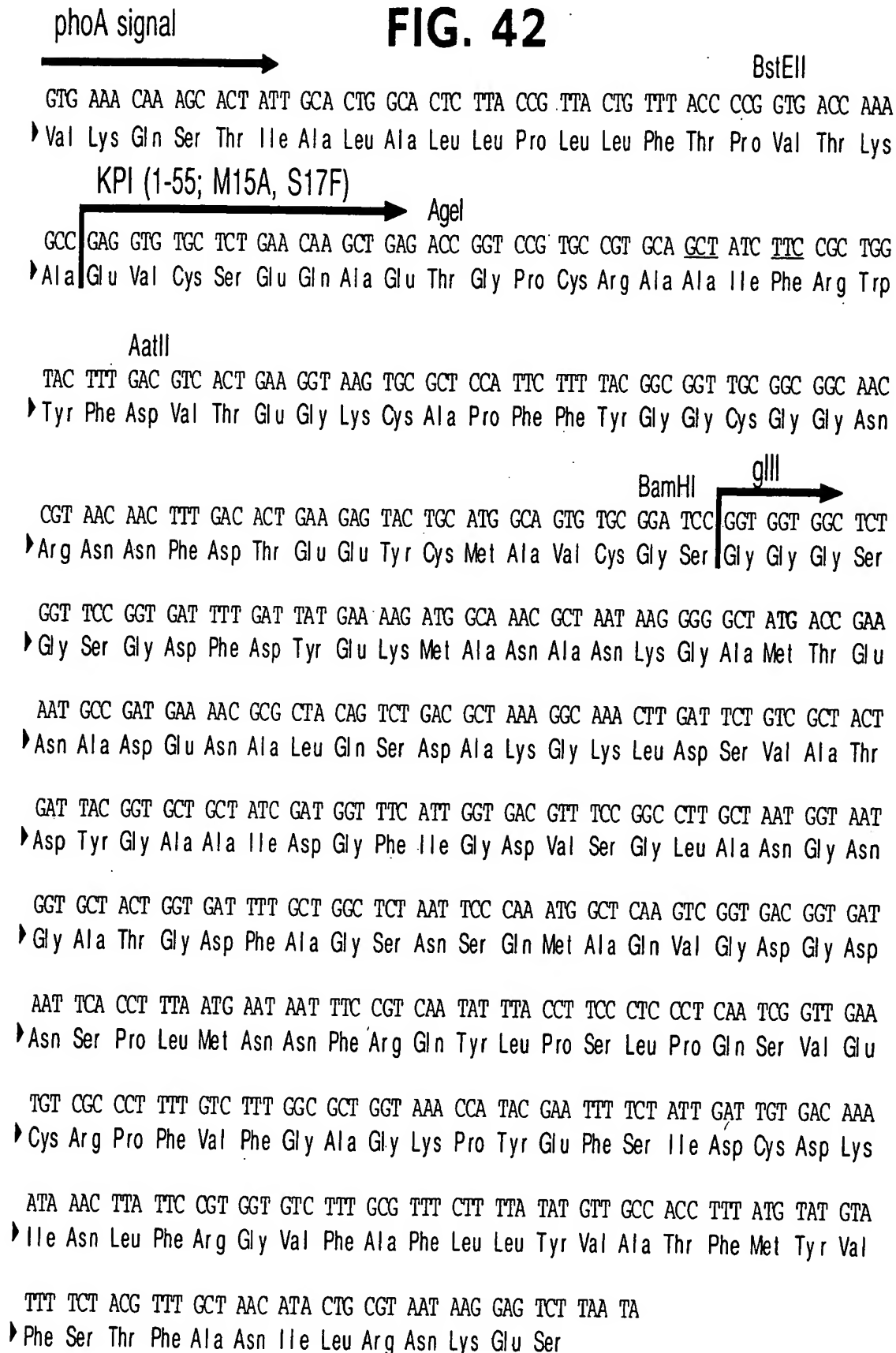
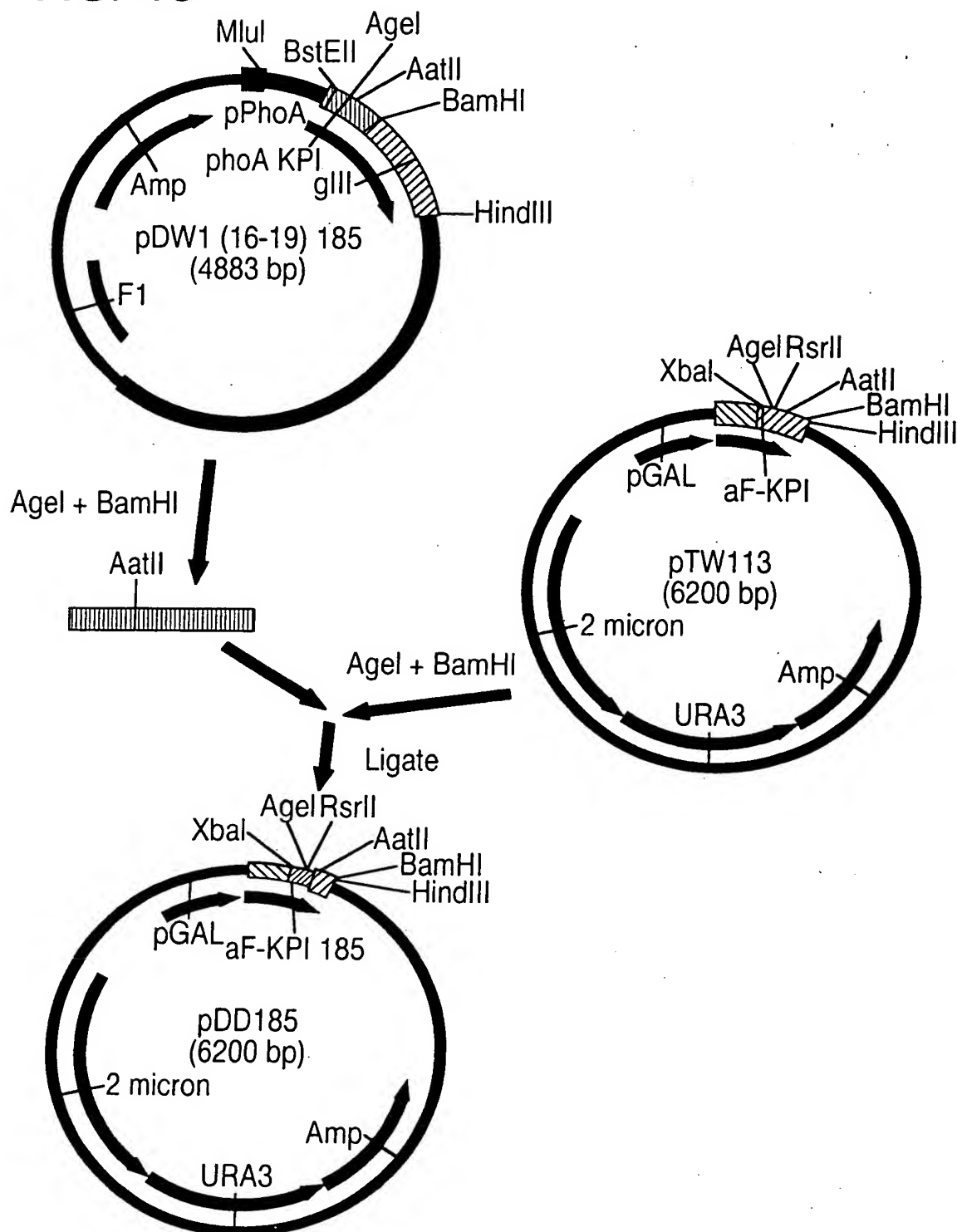




FIG. 43





pDD185

FIG. 44

α -factor



ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA

► Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG

► Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG

► Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT

► Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

KPI(-4-57; M15A, S17F)

XbaI



GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT

► Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TTC CGC TGG TAC TTT GAC GTC ACT GAA
CGA CTC TGG CCA GGC ACG GCA CGT CGA TAG AAG GCG ACC ATG AAA CTG CAG TGA CTT

► Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Phe Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG

► Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A

► Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



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FIG. 45
Plasma kallikrein inhibition by KPI (-4-57) variants

<u>Variant</u>	<u>Substitution</u>			<u>K_i(nM)</u>
	15	16	17	
TW113	KPI (-4-57)			45.00
DD185	KPI (-4-57; M15A, S17F)	A	F	0.39
TW6165	KPI (-4-57; M15A, S17W)	A	W	0.65
TW6166	KPI (-4-57; M15A, S17Y)	A	Y	0.40
TW6175	KPI (-4-57; M15L, S17F)	L	F	0.50
BG028	KPI (-4-57; M15L, S17Y)	L	Y	1.10
TW6183	KPI (-4-57; I16H, S17F)		F	1.20
TW6184	KPI (-4-57; I16H, S17Y)		Y	0.91
TW6185	KPI (-4-57; I16H, S17W)		W	1.30
TW6173	KPI (-4-57; M15A, I16H)	A		1.00
TW6174	KPI (-4-57; M15L, I16H)	L		0.90



FIG. 46A

Variant	Sequence	Inhibition Ki (nM)			
		kallikrein	Plasmin	XIIa	Xa
Aprotinin	RPDFCLEPPYTGPCAKARIIRYFYNKAGLQTFVYGGCRKRNNFSAEDCHRTCGGA	20.00	0.23	5000.0	
Aprotinin R15, S42	DFCLEPPYTGPCAKARIIRYFYNKAGLQTFVYGGCRKSNPKSAEDCHRTCGGA	0.91	0.17	3983.0	
KPI (-4-57)	EVRVVCSEQAETGPCRAHISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI	45.00	34.00	3718.0	161.0
TW6167	EVRVVCSEQAETGPCRAHISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI	61.00		3641.0	288.0
BG031	EVRVVCSEQAETGPCRAHISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI	34.00		498.0	
BG032	EVRVVCSEQAETGPCRAHISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI	49.00		731.0	
TW101	EVCSEQAETGPCRAHISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI	2000.00	11.50		
TW6208	EVRVVCSEQAETGPCRGRHISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI			369.0	
TW106	EVCSEQAETGPCRARISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI	560.00	3.70		
DD108	EVRVVCSEQAETGPCRAAISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI	1.70	11.20	1600.0	123.0
DD109	EVRVVCSEQAETGPCRAISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI	9.50		1681.0	421.0
DD110	EVRVVCSEQAETGPCRALISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI	2.10		624.0	55.0
DD111	EVRVVCSEQAETGPCRASISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI	5.60			
DD112	EVRVVCSEQAETGPCRAVISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI	6.80		998.0	
TW6179	EVRVVCSEQAETGPCRAGISRWFVDVTEGKCAPFFYGGCGNRNRPDTEEYCHAVCGSAI	78.00		368.0	



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FIG. 46B

TW6163	EVVREVCSEQAETGPCRAMHSRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	4.70	103.58	4532.0	457.0
TW6172	EVVREVCSEQAETGPCRAMASRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	315.00			1463.0
TW6180	EVVREVCSEQAETGPCRAMFSRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	70.00		885.0	39.0
TW6181	EVVREVCSEQAETGPCRAMKSRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	150.00		1514.0	
BG001	EVVREVCSEQAETGPCRAMLSRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	38.00	10.00	489.0	204.0
TW116	EVCSEQAETGPCRAMIIRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	145.00	89.00		806.0
DD102	EVVREVCSEQAETGPCRAMIPRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	16.00		315.0	
DD103	EVVREVCSEQAETGPCRAMIFRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	17.00		2128.0	110.0
DD104	EVVREVCSEQAETGPCRAMIYRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	15.00		237.0	345.0
DD105	EVVREVCSEQAETGPCRAMIWRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	18.00		198.0	320.0
TW6168	EVVREVCSEQAETGPCRAMILRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	25.80		3521.0	395.0
TW6182	EVVREVCSEQAETGPCRAMIHRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	36.00		732.0	
TW6194	EVVREVCSEQAETGPCRAMIERWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	70.83			
TW6210	EVVREVCSEQAETGPCRAMIQRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	54.00		277.0	
CL006	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI	110.20		89600.0	133.0
BG012	EVVREVCSEQAETGPCRAMISTWYFDVTEGKCAPFFYGGCGNRNPNFTTEYCHAVCGSAI			40.0	116.0



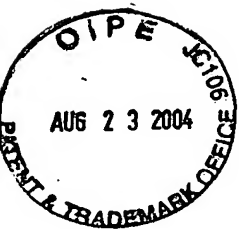
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FIG. 46C

TW6209	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	81.00	45.90	184.0	613.0
TW6211	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	184.00		402.0	
DD128	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	44.00			37.0
TW6142	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	18.00	18.00	7972.0	225.0
AL301	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	216.00		1557.0	
AL302	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	39.00			316.0
TW6147	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	35.00		1090.0	179.0
TW6138	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	18.00		921.0	309.0
TW6154	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	11.00		915.0	39.0
TW6155	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	11.00			27.0
TW6140	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	35.00		475.0	
TW6156	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI				
TW6141	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	42.00			
TW118	EVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	6.00	24.00	13009.0	68.0
DD100	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	15.00			
TW6157	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	40.00		511.0	168.0
TW6158	EVRVVCSEQAETGPCRAHISRHYFDVTEGKCAPFYGGCGNRNPNFTBYYCHAVCGSAI	29.00			



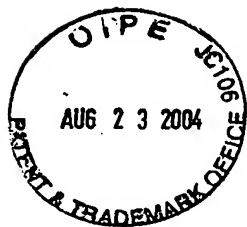
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FIG. 46D

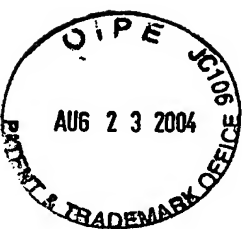
TW6159	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	17.00			64.0
TW6161	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	7.50	18.00	1507.0	8.7
DD101	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	64.00		924.0	
TW6151	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	163.00		1162.0	954.0
TW6139	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCHGNRNNFDTEBYCHAVCGSAI	19.00	22.80	152.0	78.0
TW6153	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCIGVGNRNNFDTEBYCHAVCGSAI	11.20	21.30	65.0	36.0
TW122	EVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	32.00	27.00		581.0
TW6178	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	16.00		444.0	
TW6148	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	40.00			
TW124	EVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	64.00	48.00		
TW6149	EVVREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	54.00			
TW6173	EVVREVCSEQAETGPCRAHSRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	1.00	7.24	1432.0	
TW6174	EVVREVCSEQAETGPCRALHSRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	0.90	6.89	2796.0	
BG002	EVVREVCSEQAETGPCRALLSRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	0.98	19.00	403.0	60.0
DD129	EVVREVCSEQAETGPCRALFSRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	3.60		1864.0	6.0
DD185	EVVREVCSEQAETGPCRAAIFRWYFDVTEGKCAPFFYGGCGVGNRNNFDTEBYCHAVCGSAI	0.39	8.71	150.0	196.0



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FIG. 46E

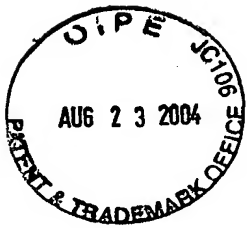
TW6165	EVRVCSQAETGPCRAAIIHRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	0.65	16.40	206.0	
TW6166	EVRVCSQAETGPCRAAIIHRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	0.4	10.10	73.0	
BG028	EVRVCSQAETGPCRALIIRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	1.10	12.10	93.8	
TW6169	EVRVCSQAETGPCRALIIRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	1.20		619.0	111.0
DD113	EVRVCSQAETGPCRALIIRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	0.85	12.80	293.0	74.0
TW6175	EVRVCSQAETGPCRALIIRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	0.50	7.46	35.0	56.0
TW6201	EVRVCSQAETGPCRAGIIRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	34.60		419.0	
TW6202	EVRVCSQAETGPCRAGIIRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	128.50		1237.0	
TW6203	EVRVCSQAETGPCRAGIIRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	31.20		5045.0	
TW6204	EVRVCSQAETGPCRAAIIHRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI			147.0	87.0
TW6205	EVRVCSQAETGPCRALISAHYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI			195.0	29.0
DD114	EVRVCSQAETGPCRAAIIHRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	0.70	7.77	224.0	
TW6190	EVRVCSQAETGPCRAAIIHRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	0.83	52.20	589.0	1396.0
TW6183	EVRVCSQAETGPCRAHHRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	1.20	11.68	12440.0	159.0
TW6184	EVRVCSQAETGPCRAHHRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	0.91	11.96	14000.0	214.0
TW6185	EVRVCSQAETGPCRAHHRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	1.30	18.60	388.0	473.0
BG003	EVRVCSQAETGPCRALIHRNYFDVTEGKCAPFFYGGCGGNRNNFDTBEYCHAVCGSAI	36.00		467.0	



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FIG. 46F

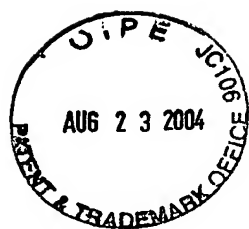
TW6186	EVRVCSQAETGPCRAHSHRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	0.48	8.86	186.0	11.0
TW6187	EVRVCSQAETGPCRAMIFRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	3.80	15.40	92.0	15.0
TW6188	EVRVCSQAETGPCRAMIYRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	4.00		419.0	24.0
TW6189	EVRVCSQAETGPCRAMIWRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	4.00			34.0
TW6170	EVRVCSQAETGPCRALILRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	2.50			452.0
DD115	EVRVCSQAETGPCRGYITRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI			213.0	299.0
DD170	EVRVCSQAETGPCRALHNRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	0.99	18.00	550.0	
TW6176	EVRVCSQAETGPCRAAHFRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	3.50	118.00	56.0	
TW6177	EVRVCSQAETGPCRALHFRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	7.20	32.70	245.0	156.0
BG006	EVRVCSQAETGPCRAALFRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	0.30	12.10	80.0	
DD130	EVRVCSQAETGPCRALFTRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	5.50			9.5
DD131	EVRVCSQAETGPCRALFKRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	7.90	2.00	1385.0	3.3
DD132	EVRVCSQAETGPCRAPFRWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	112.00			16.8
DD120	EVRVCSQAETGPCRAAFSAWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	8.30			11.0
DD121	EVRVCSQAETGPCRALLSAWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	19.00			21.0
BG014	EVRVCSQAETGPCRALIHWYFDVTEGKCAPPFYGGCGGNRRNFPDTEEYCHAVCGSAI	9.20	18.70	18.0	



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FIG. 46G

DD122	EVVREVCSEQAETGPCRALIPAWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	15.00			46.0
BG015	EVVREVCSEQAETGPCRALIYHWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	6.00	12.20	19.4	597.0
BG020	EVVREVCSEQAETGPCRAAIHKWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	1.70		106.0	
BG022	EVVREVCSEQAETGPCRAAIYHWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	0.64	7.26	14.5	
BG023	EVVREVCSEQAETGPCRALIQHWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	23.00		262.0	
BG024	EVVREVCSEQAETGPCRALIYKWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	4.10	7.47	38.7	
BG027	EVVREVCSEQAETGPCRAAIQHWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	5.80		144.0	
DD116	EVVREVCSEQAETGPCRAAIPRWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	0.14		583.0	84.0
TW6191	EVVREVCSEQAETGPCRAAIPRWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	0.26		664.0	20.0
DD117	EVVREVCSEQAETGPCRALIPRWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	0.11		1034.0	99.0
BG029	EVVREVCSEQAETGPCRALIYHWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	3.20		7.9	
BG030	EVVREVCSEQAETGPCRALIYHWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	4.60		26.1	
BG033	EVVREVCSEQAETGPCRAAIYHWYFDVTEGKCAPFFYGGCGNRNNFDTEEYCHAVCGSAI	0.75		5.6	



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FIG. 46H

BC034	EWREVCSEQAETGPCRAAIYHMYFDVTEGKCAPFFYGGCGNRNFFDTEEYCHAVCGSAI	0.47		18.5
BC040	EWREVCSEQAETGPCRALIYHMYFDVTEGKCAPFFYGGCGNRNFFDTEEYCHAVCGSAI	3.40		8.6
BC016	EWREVCSEQAETGPCRGAIQHMYFDVTEGKCAPFFYGGCGNRNFFDTEEYCHAVCGSAI	160.00		178.0
BC017	EWREVCSEQAETGPCRGAIIRHMYFDVTEGKCAPFFYGGCGNRNFFDTEEYCHAVCGSAI	180.00		200.0
BC021	EWREVCSEQAETGPCRGSIIRHMYFDVTEGKCAPFFYGGCGNRNFFDTEEYCHAVCGSAI	340.00		224.0
BC025	EWREVCSEQAETGPCRGILYHMYFDVTEGKCAPFFYGGCGNRNFFDTEEYCHAVCGSAI	65.00		16.2
BC026	EWREVCSEQAETGPCRGAIYHMYFDVTEGKCAPFFYGGCGNRNFFDTEEYCHAVCGSAI	50.00		34.9
DD118	EWREVCSEQAETGPCRALHNRWYFDVTEGKCAPFFYGGCGNRNFFDTEEYCHAVCGSAI	0.53		
DD134	EWREVCSEQAETGPCRALFKRWYFDVTEGKCAPFFYGGCYGHRNFFDTEEYCHAVCGSAI	1.10	1.05	15640.0
DD135	EWREVCSEQAETGPCRALFKRWYFDVTEGKCAPFFYGGCLGHRNFFDTEEYCHAVCGSAI	1.30		7473.0
DD136	EWREVCSEQAETGPCRALFKRWYFDVTEGKCAPFFYGGCMGHRNFFDTEEYCHAVCGSAI	1.10		1.8

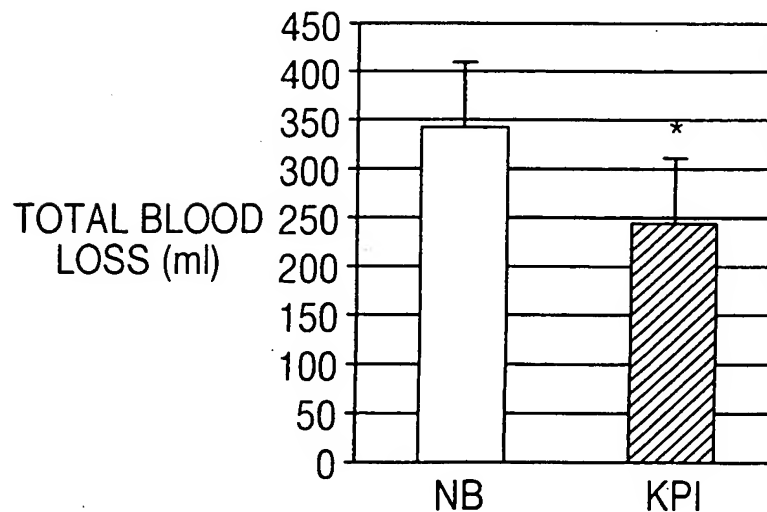


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FIG. 47

VOLUMES

NS	344.25	
KPI	245.75	
	KPI	NS
	298	366
	266	342
	354	294
	258	385
	168	288
	266	469
	172	338
	184	272
MEAN	245.75	344.25
STDEV	66.2414415	63.97488346
TTEST		0.009094999





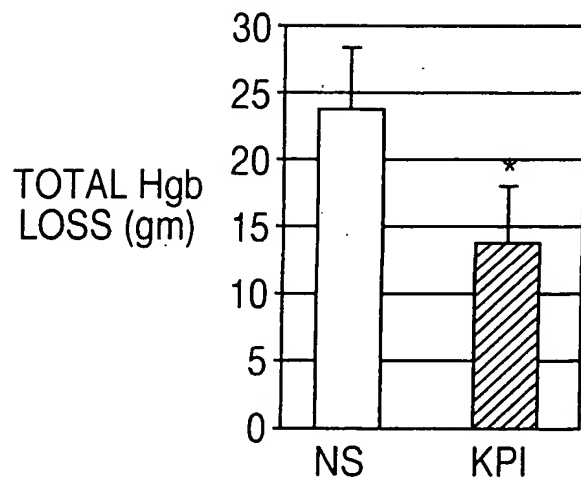
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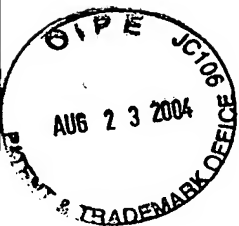
FIG. 48

HEMOGLOBIN

NS	23.61
KPI	13.59

	KPI	NS
	16.58	24.95
	15.19	24.87
	20.21	20.46
	8.99	27.59
	14.63	18.23
	15.31	31.59
	7.7	23.26
	10.14	17.96
MEAN	13.59375	23.61375
STDEV	4.261438	4.68761
TTEST		0.000536





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FIG. 49

PaO₂

	Baseline PaO ₂		End CPB		Obs 60 min		Obs 180 min	
	KPI	NS	KPI	NS	KPI	NS	KPI	NS
	652.2	670.9	495.7	60.5	483.7	441.3	391.3	
	654	559.2	444.6	132.2	330.1	448.7	264.1	484.6
	596.2	622.9	170.2	93.8	415.4	85.1	416.5	81.3
	606.2	689.2	264.2	333.9	430.2	529.6	361.9	333.2
	633.1	665.1	567.2	341.7	613	568.3	90.8	546.6
	646.6	527	507.4	226.9	564.3	438.1	518.2	485.3
	563.2	461.7	547.1	89.1	501	42.6	494.2	45.6
	659.9	508	416.6	59.7	504.5	405.8	452	383.7
MEAN	626.425	588	426.625	167.225	480.275	369.938	371.1	344
STDEV	34.4692	85.5055	140.474	117.993	88.6187	196.523	150.277	186.22
TTEST	3	6	1	1	9	5	4	7
	p=	0.268	p=	0.0014	p=	0.17915	p=	0.76

N.S.

N.S.

FIG. 50

Summary of Data

Total Volumes

	Total volume loss	Total Hgb Loss
KPI-1	298	16.58
KPI-2	266	15.19
KPI-3	354	20.21
KPI-4	258	8.99
KPI-5	168	14.63
KPI-6	266	15.31
KPI-7	172	7.7
KPI-8	184	10.14

MEAN	245.75	13.59
STDEV	66.24	4.26

NS-1A	366	24.95
NS-2	342	24.87
NS-3	294	20.46
NS-4	385	27.59
NS-5	288	18.23
NS-6	469	31.59
NS-7	338	23.26
NS-8	272	17.96

MEAN	344.25	23.61
STDEV	63.97	4.69

*p = 0.009

*p = 0.0005

Serial Chest tube Hbg

	0-30min	30-60min	60-120min	120-180min
	3.7	4.3	8.6	6.2
	4.3	6.4	6.7	5.7
	4.1	4.4	7	7.1
	2.8	4	4.4	1.9
	6.3	6.5	7	6.7
	4.1	6.1	5.6	6.3
	3.1	4.6	5.4	4.4
	6.9	5.8	5.4	4.2

MEAN	4.41	5.26	6.26	5.3
STDEV	1.45	1.04	1.32	1.72

	7.7	8.6	6.1	5.4
	7.2	7.4	7.6	7.1
	5.4	7.5	7.5	6.5
	8.4	7.2	7.1	6.3
	7.5	7.2	5.2	5.6
	4	7	7.3	7.4
	7.5	7.7	5.8	4.2
	7.4	8.2	6	5.3

MEAN	6.89	7.6	6.58	6.1
STDEV	1.44	1.04	0.91	0.85

*p = 0.004

*p = 0.002

NS

NS

